

REMARKS

Independent claims 1 and 14 have been amended to include the subject matter of dependent claim 4. Claim 4 has been amended, and new claim 24 has been added to recite the use of a numerical aperture of greater than or equal to 1.2 based on the support found in the present specification at ¶32. No new subject matter has been added. No new issues are presented as the subject matter of claim 4 was previously considered by the examiner.

Basic 103 Rejection – Admitted Prior Art In View Of Heid et al. and Neev et al.

Claims 1-22 are rejected under 35 U.S.C 103(a) over the background art identified in the specification (AAPA) in view of newly cited art Heid et al. (US 2008/0220469) and Neev et al. (US 5,720,894). Four additional rejections cite additional tertiary references to buttress this basic combination of art in rejections of groupings of dependent claims 10-13 and 19-22. Applicants respectfully traverse.

The background of the invention that is acknowledged to be prior art is found in paragraph nos. 2-10. In summary, this background recognizes that blade-based microtomes have been used to remove thin slices of tissue with a sliding carriage device. Use of a blade, however, requires additional steps when soft tissue is involved. Methods for stabilizing soft tissue includes freezing and impregnating with a liquid that will impart greater integrity to the sample but at the cost of disadvantages for sample integrity, cost and preparation time. Lasers have been used for microdissection, i.e., transversely cutting the slice coming from the blade-based microtome into smaller pieces. In this context, the present invention replaces the blade-based microtome with a laser microtome thereby avoiding the need for external stabilizing agents with the associated procedures and impacts on sample integrity.

Heid et al. (US 2008/0220469) discloses a method for identifying tissue slice supports. In ¶18, as cited by the examiner, Heid et al. notes that the disclosed invention “does not depend on the manner in which the tissue sample is treated and cut.” This explains why both knives and laser microtomes may be useful (penultimate sentence in ¶18) in connection with the disclosed invention. Heid et al. provides no detail, however, of how a laser-based microtome is constructed or operated to produce tissue samples.

Neev et al. (US 5,720,894) discloses a pulsed laser as a replacement for a dental drill (col. 54, lines 29-31). As noted in col. 4, lines 31-35, the ultrashort (femtosecond) pulsed laser is used to selectively ablate undesired material at a removal rate that meets or exceeds that of a drill. The benefits of a very short pulse time are disclosed at cols. 7+ and relate primarily to the avoidance of thermal loading associated with lasers of longer pulse duration (i.e., in the nanosecond realm). The advantages of material removal efficiency and minimal collateral damage are summed up in col. 11 at lines 39-51.

Neev et al. discloses in col. 13, lines 58-60, that a “typical focusing element may consist of a simple large f-number ($f>100$) singlet lens for focusing the beam onto the target area in a spot size of greater than 250 micrometers.” Neev et al. does not qualify, further describe or define optics of the system. There is no working example.

ARGUMENT

The references asserted by the examiner both alone and in the various combinations presented fail to disclose a laser-based microtome system having a numerical aperture of greater than or equal to 0.65.

The background of the technology recited in the present specification (denoted as “AAPA” by the examiner) does no more than acknowledge the conventional use of a blade-based microtome and associated problems. The background section does not acknowledge that laser-based microtomes exist or acknowledge that those in the art knew how to operate a conventional laser as a microtome as claimed.

Heid et al. provides no more than passing mention that lasers may be used for producing tissue slices. The devil is always in the details, and Heid et al. fails to provide the critical teachings of how such a process could be accomplished. Heid et al. does not disclose either the use of pulsed laser or an aperture number of greater than or equal to 0.65. The background art of the present specification and Heid et al. thereby fail to present the required *prima facie* case of obviousness.

The dental ablation system as disclosed by Neev et al. does not fill in the gaps missing from the combination of the acknowledged use of a blade-based microtome and the teachings of Heid et al. First, area ablation on tooth surfaces or surgical procedures suggested by Neev et al.

are not the same as, or suggestive of, microtomy as disclosed in the present specification.

Nothing cited by the examiner or provided as a rationale in the Final Action provides a *prima facie* case of obviousness from such a connection.

Second, the disclosure in Neev et al. regarding “a simple large f-number ($f > 100$)” is unclear and cannot render *prima facie* obvious the claimed use of a numerical aperture of greater than or equal to 0.65. Pointedly, use of term the “f-number” and the abbreviation “ $f > 100$ ” confuses two standard designations of optical art without any way to figure out what Neev et al. meant by such disclosure.

An *aperture* describes the width of the opening of an optical system through which light of the system is directed. An aperture is usually abbreviated with the letter “D” and describes, for instance, whether a large or small lens is used in a single lens system.

Focal length of an optical system is usually abbreviated by lowercase “f” and can be used to describe the distance between a lens and a focal point. The focal length may be used to determine whether a strong or soft lens is to be used in a single lens system.

The *f-number* (F# or f-stop) is used to denote the ratio of focal length to aperture size and is a dimensionless quantity that is related to the angle of convergence in a cone of focusing light emanating from a circular aperture. The common form is:

$$F \# = \frac{f}{D}$$

where f is the effective focal length of a focusing optical system and D is the system’s circular entrance pupil diameter. See, <http://www.great-landscape-photography.com/aperture.html> attached as Exhibit A and “F-Number, Numerical Aperture, and Depth of Focus”, Encycl. of Optical Engineering, pp. 556-558 (2003) attached as Exhibit B.

The use by Neev et al. of both designations and the failure to define the scope of “large” would not have rendered obvious the use of an aperture of greater than or equal to 0.65 (claim 1) or greater than or equal to 1.2 (amended claim 4). It is mathematical fact that aperture values and f-numbers have an inverse relationship in that an aperture value of greater than 1.0 will reflect increasingly smaller values of the f-number, contrary to a teaching in favor of “large” f-numbers which prefer ever decreasing aperture values.

Moreover, Neev et al. fails to disclose that any aperture value could be used to make a laser-based microtome in which the short depth of field is used to minimize damage to tissues at

the precise focal point of the laser system where threshold energies cut the tissue. Such uncertainty and gaps of disclosure with respect to the claimed aperture cannot properly support a finding of *prima facie* obviousness under §103.

None of the tertiary references cited by the examiner teach or suggest a laser microtome having the claimed aperture range.

Launay et al. US 5,241,607 is directed to a method for providing spatial orientation markings on samples to permit serial sections to be compared in overlay orientation as a way to correct for deformations during microtomy. The only mention of a pulsed laser is in col. 1 at line 67 in connection with boring a hole through the thickness of the uncut sample. There is no teaching or disclosure that a laser should be used for microtomy or that such a laser should have an aperture number of greater than or equal to 0.65.

Michel US 4,638,800 describes a laser-based arthroscopic surgery device for a CO₂ laser. The desired uses for the system are disclosed in col. 2 at lines 49-56 and include (a) removing tissue from joints, (b) debriding and polishing areas of bone or tissue, and (c) creating contoured sockets for a prosthesis. Microtomy and thin section slicing are not among the disclosed uses. The optical concerns of focal length and focus are described in cols. 6-8 but do not mention an aperture value or one of greater than or equal to 0.65 or the advantages of using such an aperture for a pulsed laser microtome.

Ream US 5,827,313 teaches a catheter system for guiding ultrasound transducers, imaging devices (optical fibers and laser tomography imagers), artherectomy cutters within a patient. Optical coherence tomography (OCT) catheters are described in detail in col. 7 at lines 60+. Tomography is not, however, the same as the removal of a thin sample by microtomy. There is no mention of a suitable aperture number for a pulsed laser microtome.

Zundel US 4,132,328 concerns a replacement for conventional pull-tab cans with a non-detachable opening scheme. There is no mention of pulsed lasers or microtomy that could help present a *prima facie* case of obviousness with the other cited references.

Applicant submits that this Amendment After Final Rejection places this application in condition for allowance by amending claims in manners that are believed to render all pending claims allowable over the cited art and/or at least place this application in better form for appeal.

In re Application of:
Omid KERMANI
Application No.: 10/541,248

Atty. Dkt. No. 49102

Reconsideration and allowance are courteously solicited.

Dated: May 12, 2009



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EXHIBIT A

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Lens Aperture

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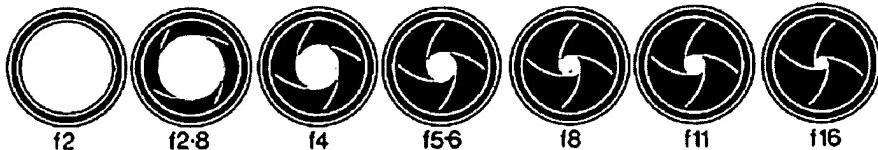
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The aperture of a lens determines the amount of light that passes through the lens to the film or digital sensor. It's a diaphragm of overlapping leaves that is either controlled by an external ring on older lenses or set by controls on the newer cameras which sets the lens electronically.

In the case of older cameras and lenses, turning the ring one way opens up the lens so there's no obstruction to incoming light. Turning it the other way closes down the lens until only a small circular opening is left for the light to pass through.



With newer cameras, buttons or a dial on the camera will let you set the appropriate aperture. However, unless there's a depth of field preview button, you may not see any change. The camera will close the lens down to the value you've set just before it takes a photo.

f-Stops

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On all lenses, aperture is calibrated using what are called **f-stops** (in fact, the terms are almost interchangeable). Along with the focal length of the lens, the maximum aperture is usually used to specify a lens. By that I mean that if the lens is described as an f/2.8 or an f/4 lens, for instance. The actual range of f-stops varies between lenses but the sequence is always the same:

f/1, f/1.4, f/2, f/2.8, f/4, f/5, f/5.6, f/8, f/11, f/16, f/22, f/32, f/45, f/64

Maximum apertures can be "non-standard" - that is, not in the above list, so it's common to see short focal length zoom lenses with wide open settings of f/3.5. Longer focal length zooms may have maximum values of f/4.5.

Standard lenses, sometimes known as "fixed" lenses (i.e. they don't zoom), tend to have higher maximum f-stops than zoom lenses. On film SLRs (Single Lens Reflex), the standard 50mm lens that comes with the camera will have a wide open setting of f/2, f/1.8 or even f/1.4.

Regardless of the focal length of the lens or the diameter of the lens, f-stops denote relative apertures. - they actually specify the ratio of the diameter of the aperture to the focal length of the lens.

Let's take an example. On a 135mm telephoto lens (good for isolating something in the distance), an aperture setting of f/4 means that the physical diameter of the diaphragm opening is 33.75mm. How did I get this figure? Divide the focal length of the lens by the f-stop. So, $135 / 4 = 33.75$.

On a 28mm lens (great for wide landscape photos) with its aperture set to f/4, the size of the opening will be 7.5mm ($28 / 4 = 7.5$).

That's Neat!

Here's what's neat about this system: The amount of light that can pass through a lens decreases proportionally with increasing focal length - basically, the longer the focal length, the less light gets through the lens. Using the aperture system outlined above allows you to change lenses, keep the same f-stop between lenses and still get the same exposure. If you keep all the camera/lens settings the same (aperture, shutter speed, film speed) your exposure will remain the same and the only thing that changes is what you see through the lens - more or less of the landscape you're photographing.

If you're mathematically minded, you probably noticed that each successive f-stop is the square-root-of-2 (approx. 1.414) times the previous f-stop.

Decreasing your f-stops double your exposure. For example, if your exposure is 1/125 sec at f/5.6 and you change your aperture to f/8 need to double your shutter speed to 1/60 sec. If you changed to f/8, you'd need to double your shutter speed

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Likewise, increasing your f-stops halves your exposure for each f-stop. So, changing from f/4 to f/2.8 would mean halving your shutter speed from 1/125 sec to 1/250 sec.

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Simple Rules

So, two simple rules of thumb to get the same exposure are:

- **double your shutter speed for each decrease in f-stop**
- **halve your shutter speed for each increase in f-stop**

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EXHIBIT B

“F-Number, Numerical Aperture, and Depth of Focus”,
Encycl. of Optical Engineering, pp. 556-558 (2003)

F-Number, Numerical Aperture, and Depth of Focus

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INTRODUCTION

F# is a term widely used in optics which often appears in calculations for first-order parameters, diffraction effects, depth of focus, and radiometric energy transfer. However, the *F#* is only a derived quantity with significant limitations regarding its accuracy and recommended uses. Related parameters include the *TW* and numerical aperture (NA). The depth of field of a system may or may not be limited by the optical diffraction limit (and hence the *F#*), therefore a detailed discussion of alternative calculations for this parameter is included.

F-NUMBER

The *f-number*, sometimes written *F#* or referred to as the *f-stop*, is a dimensionless quantity related to the angle of convergence in a cone of focusing light emanating from a circular aperture. Because this term is a frequently misused or misinterpreted, it is important to review its usage within the context of any optical presentation. Unfortunately, the exact definition varies depending on the application, but the most common form is

$$F\# = \frac{f}{D}$$

where *f* is the effective focal length of a focusing optical system and *D* is the system's circular entrance pupil diameter. It is important to note that *F#* is a derived quantity, dependent upon other more fundamental system parameters. It is also worth noting that its dependence on the effective focal length *f* renders the *F#* valid only when a collimated plane-wave (infinite object) happens to be the system input. The *F#* is not defined for an afocal system, which ideally has collimated plane-wave input and output. For image relay systems with finite object and image distances, the angular convergence of the focal cone will likely vary with object or screen distance, and thus the meaning of any stated *F#* would in this case require additional qualifications. The *F#* typically varies across the image plane height of any given objective lens assembly, as it is often unique to each position within the

field of view because of vignetting and angular projection geometry. For systems with noncircular apertures, the *F#* is again not clearly defined, and typically a statement indicating the effective length of any particular aperture dimension of interest must be made. The *F#* is also inadequate to describe the properties of apodized systems or Gaussian laser beam delivery.

In diffraction calculations for circular apertures, the ratio of *fD* occurs frequently and therefore the *F#* is often substituted for convenience. For example, the diffraction limited cutoff frequency of the modulation transfer function (MTF) for an incoherent system with a circular aperture is given by $f_c = 1/\lambda F^2$, in units of line pairs per millimeter (lp/mm) when the wavelength λ is given in millimeters. By simple trigonometry, the angular relation of *F#* to the half-angle *U* of the cone of focusing light in an optical system is tangential since $\tan(U) = D/2f$. Thus, *F#* is inversely proportional to the tangent of the focusing cone half-angle, meaning that smaller values of *F#* indicate steeper cone angles. For a fixed aperture diameter *D*, an increase in focal length *f* results in a smaller convergence angle *U* and hence a larger *F#*. Likewise, for a fixed focal length *f*, an increase in aperture *D* results in a steeper angle *U* and a lower value of *F#*. In photography, the steepness of angle *U* is referred to as the "speed" of the objective lens, or perhaps more accurately, the exposure time needed by the film behind the lens. A lens operating at *F#*1.0 is considered "fast," whereas the order of *F#*12.0 might be considered "slow." This tangential relationship often leads to the misuse of *F#* for radiometric calculations, wherein photon flux is proportional to the solid angle of collection by the optical system. The problem is that the solid angle does not exactly obey the tangent law. For a Lambertian source object of radiance *L*, the irradiance *E* at the focal point of a circular aperture optical system in air is given by¹¹

$$E = \pi L \sin^2(U) \approx \frac{4\pi L}{F^2 f^2}$$

As long as $\tan(U) \approx \sin(U)$, the *F#* provides an easily calculated, approximate relation to the square root of the system irradiance. For fast *F#*'s on the order of *F#*1.0 however, the error in this approximation increases rapidly. For example, if given a true cone half-angle of *U*=30°, the error between $\sin^2(U)$ and $\tan^2(U)$ is ap-

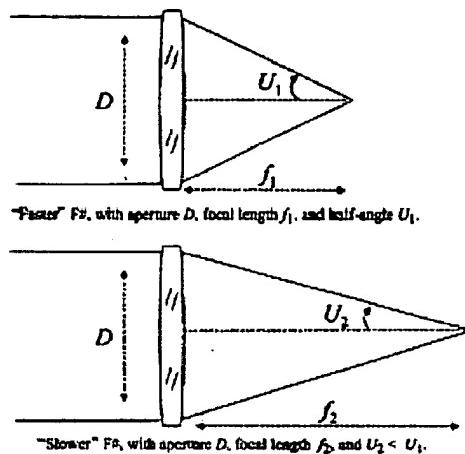


Fig. 1 Illustration of fast and slow F#s.

proximately 33%. Once *F*# reaches 2.35 and above, the error quickly settles to less than 5%. Despite this error margin, it is a common practice in photographic objectives to feature *f*-number positions marked 1.4, 2.0, 2.8, 4, 5.6, etc., as each represents roughly a doubling of the irradiance on the film.^[2] The higher the irradiance, the less time is needed for film exposure, and the faster the shutter speed may be used in the camera (Fig. 1).

In low-light level imaging applications, a variant of the *F*# known as the *TW* is sometimes encountered. *TW* is simply *F*# divided by the square root of the optical transmission *T_{obj}* of the objective optics.^[3]

$$T\# = \frac{F\#}{\sqrt{T_{obj}}}$$

For example, an objective lens focused at infinity with a circular aperture diameter *D*=25 mm and an effective focal length *f*=28 mm would have an *F*#=1.12. If the lens transmitted 84% of the incoming radiation (with losses perhaps as a result of reflections on the coated surfaces and absorption within the glass), then the effective *TW* for the objective would be *TW*=1.22. It is not physically possible for the *TW* value to be less than that of the *F*#.

NUMERICAL APERTURE

The NA of a focal optical system is defined as the sine of the half-angle *U* of the cone of rays coming to a focus,

multiplied by the refractive index *n* of the medium in which focus occurs:

$$NA = n \sin(U)$$

This quantity is independent of wavefront entrance conditions on the optical system and does not require knowledge of either the aperture diameter *D* or focal length *f*, but it does assume a circular aperture and noncollimated output. The NA is directly proportional to the square root of the image irradiance without approximation, and is therefore frequently used in radiometric calculations for fiber optics and microscope objectives. The NA can also be used to define the maximum cone angle of rays which leave an object and enter an optical system. In practice, a *NA*>0.95 rate in air (*n*≈1) is very difficult to achieve, so microscopists who require better performance have obtained NAs as high as 1.4 to 1.6 by immersing the sample in oil (*n*≈1.51).^[4]

DEPTH OF FOCUS AND DEPTH OF FIELD

The *depth of focus* parameter refers to the amount of focal plane misplacement which does not degrade the ideal point image beyond a certain criteria. If the Rayleigh 1/4 wave criteria is assumed, a commonly accepted tolerance on image defocus Δz' can be solved geometrically as^[5]

$$\Delta z' = \pm \frac{\lambda}{2(NA)^2} \approx \pm 2\lambda(F\#)^2$$

The amount of image defocus can be converted into object displacement via paraxial optics formulae, in which case the value for the *depth of field* is solved for an object displacement of Δz. However, working with the *F*# in this case is somewhat cumbersome because this relation depends solely on the aperture diameter *D*, nominal object distance *z*, and wavelength λ as follows:

$$\Delta z = \pm 2z^2 \left(\frac{\lambda}{D^2} \right)$$

It is important to state that the *depth of field* and *depth of focus* criteria of real systems are strongly dependent on the imaging application and hardware circumstances; the Rayleigh 1/4 wave criteria is not always the best measure of optical system performance in many situations. Common examples of the inapplicability of the Rayleigh criteria exist in most commercial charge-coupled device (CCD) camera sensors, where the CCD detector pitch fundamentally limits system resolution to a value much lower than the optical spatial cutoff frequency. The optical transfer performance of these systems can be

degraded by much more than 1/4 wave before a defocused electronic image is noticeable.

DEPTH OF FIELD FOR IMAGING SYSTEMS

To explain the concept of the Rayleigh defocus criteria applied to entire imaging systems more fully, it is expedient to first detail the effects of 1/4 wave defocus on an incoherent optical system, which otherwise should be diffraction limited.¹⁶ Consider a simple optical system as shown in Fig. 2, wherein light waves from a distant point source are effectively planar once they impact a lens of finite aperture radius r , which then bends the waves back into a convergent focus. A direct interpretation of the Rayleigh criteria is that this system will remain roughly within optimal focus as long as the wavefront sag caused by changing the object distance, shown in Fig. 3, remains less than 1/4 the wavelength of light.

$$SAG = z - \sqrt{z^2 - r^2}$$

The wavefront sag results from a direct and simple trigonometric relationship between the aperture radius r and the object distance given by z , and is easily calculable. It reaches its maximum value at the aperture edge. As z decreases from infinity, the sag gradually increases. In practice, an optical system can be set for best focus not at infinity, but at an object distance of $z_{1/4}$ where the sag is 1/4 wave from an infinite plane wave. In this case, infinity objects are within a 1/4 wave sag tolerance, and closer objects will be within a + 1/4 wave sag at a distance of roughly at 0.5 $z_{1/4}$. The location $z_{1/4}$ is known as the *hyperfocal distance* setting because it optimizes the maximum *depth of field* tolerance from infinity to the nearest possible distance z .

The value of the sag is equivalent to the aberration term known as *defocus*, generally denoted by the variable w_{010} (ref. aberration polynomial). The system resolution transfer function, whether the system is a simple lens or

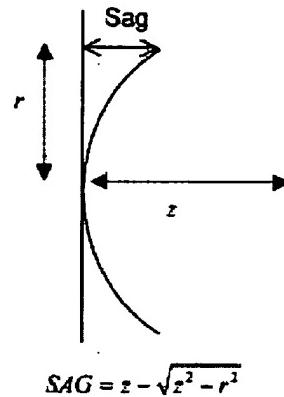


Fig. 3 Wavefront sag calculation.

an assembly containing lenses, cameras, and electronics, can be directly evaluated for varying amounts of defocus w_{010} . For a one-dimensional aperture, the modulus of the optical transfer function (OTF), often called the MTF, of defocused optics is given by the formula⁷¹

$$OTF(f_s) = \left(1 - \frac{f_s}{2f_0}\right) \text{sinc}\left(\frac{4f_s w_{010}}{\lambda f_0} \left(1 - \frac{f_s}{2f_0}\right)\right)$$

for $|f_s| \leq 2f_0$

where the normalized cutoff frequency, expressed in lp/mm, for incoherent illumination is given by $2f_0 = 1/\lambda F\#$ and the defocus aberration coefficient denoted by w_{010} may be set equal to Rayleigh's limit of $1/4\lambda$ or any other desired value. The OTF formula may then be evaluated for incremental values of spatial frequency f_s ranging from zero to the normalized cutoff mentioned above and the graphic results for various defocused, circular aperture optical MTFs are shown in Fig. 4. It is interesting to note that at a spatial frequency f_s equal 1/2 the cutoff, the amount of degradation in MTF as a result of the 1/4 wave Rayleigh criteria is equal to $2/\pi$ exactly, or about 64%. Because Nyquist theory states that perfect object reconstruction of a sampled image is possible for frequencies only up to half the system cutoff frequency, it may be desirable to consider the $2/\pi$ degradation to MTF at the half-cut-off frequency as being the definition of defocus tolerance to any system transfer function as well. The system transfer function may include not only the effects of optics, but also the detector sampling, electronics, and display parameters. The limiting system component may or may not be the optics. If the optics are the limiting factor, then the criteria of $2/\pi$ degradation to MTF at the half-cut-off frequency will result in the same Rayleigh 1/4 wave criteria solution for the *depth of field* object

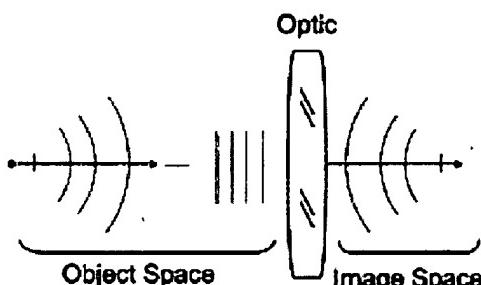


Fig. 2 Plane-wave input to optical system.